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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/865,859 | 05/25/2001 | Mary E. Gerritsen | 10466/32 | 9530 |

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EXAMINER

QAZI, SABIHA NAIM

ART UNIT PAPER NUMBER

1616

DATE MAILED: 02/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/865,859

Applicant(s)

GERRITSEN ET AL.

Examiner

Sabiha Naim Qazi

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 18 November 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 1-18 is/are pending in the application.
- 4a) Of the above claim(s) 5,7,8,11,15,17 and 18 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 1-4,6,9,10,12-14 and 16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) 5,7,8,11, are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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Claims 1-18 are pending. No claim is allowed. Amendments are entered. Claims 1-4, 6, 9, 10, 12-14, 16 are rejected; others are withdrawn from consideration as non-elected invention. Response filed in paper no.12 is hereby acknowledged. Arguments are found persuasive in-part therefore all the rejections are withdrawn except 103(a). The rejection is maintained on the same reasons as set forth in our previous office action.

Information Disclosure Statement

The information disclosure statement filed on 11/20/2002 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patent ability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

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4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

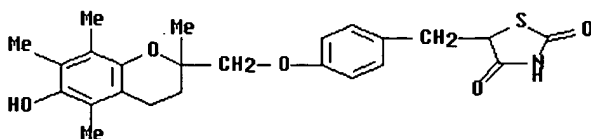
This application currently names joint inventors. In considering patent ability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1. Determining the scope and contents of the prior art.

Claims 1-4, 6, 9, 10, 12-14 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Urban et al. (5,814,647) and Cushman et al. (J. Med. Chem. (1997), Vol 40, No. 15, 2323-2334). See the entire document especially lines 1-9, col. 3; lines 13-43; examples 5, 6 and 8; and figures 11 and 13; see in Cushman et al. lines 16-23 col. 1, page 2323) where angiogenesis is defined as the formation of new blood vessels required for the growth of solid tumors.

2. Ascertaining the differences between the prior art and the claims at issue.

Instant claims differ from the reference Urban et al. in claiming a method for inhibiting "angiogenesis" by the thiazolidinedione compounds of formula 1 (elected species is troglitazone) whereas prior art teaches use of troglitazone and related thiazolidinedione compounds as PPAR gamma ligand in the treatment of cancer (lines 1-5 and 13-22, col. 3; examples 5 and 6) and climacteric. Urban et al. does not use the term "angiogenesis" as in instant claims. Following is the structure of elected species Troglitazone,



which is a benzopyran-2,4-thiazolidine dione derivative, namely (+)-5-((4-(3,4-dihydro-6-hydroxy-2,5,7,8-

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tetramethyl-2H-1-benzopyran-2-yl)methoxy)phenyl)methyl)-2,4-thiazolidione. Cushman et al. teach that angiogenesis is the formation of new blood vessels required for the growth of solid tumors, (see lines 16-23, col. 1, page 2323).

3. Resolving the level of ordinary skill in the pertinent art.

Since Cushman et al. teach that angiogenesis is the formation of new blood vessels required for the growth of solid tumors, (see lines 16-23, col. 1, page 2323).

Inhibition of angiogenesis is to stop the growth of tumor. Applicant is claiming method of inhibition of angiogenesis by troglitazone and Urban et. al. teaches troglitazone for treatment of cancer, which is the inhibition of angiogenesis. Therefore, it would have been obvious to one skilled in the art at the time of invention to be motivated to use troglitazone for treatment of cancer and for inhibition of angiogenesis because angiogenesis is the formation of new blood vessels.

No tumor will be produced if the new formation of blood vessels is stopped by troglitazone.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Since troglitazone is disclosed as a ligand for the orphan nuclear receptor PPAR Gamma. Translocation of this transcription factor in the nucleus of cells at sufficient rates inhibits transcription and reduces progesterone production in normal granulosa cells without a loss of cell viability. However, this inhibition of transcription in rapidly dividing cancer cells expressing PPAR gamma results in the loss of cell viability and inhibition of cell growth. Motivation is that Troglitazone and related compounds are disclosed for use in the treatment of cancer, to impair the growth of cancer cells without killing normal cells. See lines 40-43, col. 3 in Urban reference. One skilled in the art would use these compounds for the treatment of cancer, no matter mechanism of angiogenesis is not disclosed.

A reference is good not only for what it teaches by directs anticipation but also for what one of ordinary skill might reasonably infer from the teachings. *In re opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA 1976). A reference is not limited to working examples. *In re Fracalossi* 215 USPQ 569 (CCPA 1982). Accordingly, the burden of proof is upon applicants to show that

instantly claimed subject matter is different and unobvious over those taught by prior art. See *In re Brown*, 173 USPQ 685, 688; *In re Best*, 195 USPQ 430 and *In re Marosi*, 218 USPQ 289, 293.

In the light of the forgoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the instant claims would have been obvious within the meaning of 35 U.S.C. 103(a).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Telephone Inquiry Contacts

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sabiha Naim Qazi whose telephone number is 703-305-3910. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jose Dees can be reached on 703-308-4628. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

February 10, 2003


SABIHA QAZI, PH.D
PRIMARY EXAMINER